## *Remarks*

Applicants would like to thank Examiner Bland for taking the time to discuss the outstanding rejection with us during our recent telephonic interview. During the interview, the cited references: Pandey, Tidmarsh, and Fukuzumi were discussed. Applicants distinguished the claimed invention over the disclosures of the cited art and discussed why the claimed invention is unobvious in view the cited art.

Reconsideration of this Application is respectfully requested. Claims 1, 2 and 25 are pending in the application, with claim 1 being the sole independent claim.

Based on previously presented arguments and the following remarks, Applicants respectfully request that the Office reconsider the currently outstanding rejection, and that they be withdrawn.

***Rejections under 35 U.S.C. § 103***

The rejection of claims 1, 2, and 25 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. 2002/0198157 A1 ("Pandey") in view of U.S. Patent No. 6,989,140 B2 ("Tidmarsh") and Fukuzumi *et al.*, *J. Phys. Chem. A 106*:5105-5113 (2002) ("Fukuzumi") is respectfully traversed.

The U.S. Supreme Court has held that "[i]f a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007). The Office has the burden of establishing a *prima facie* case of obviousness. *See In re Bell*, 991 F.2d 781, 783 (Fed. Cir. 1993). The U.S. Supreme Court has affirmed that a *prima facie* case of obviousness is established by considering the factors set out in *Graham v. John Deere*. *See KSR*

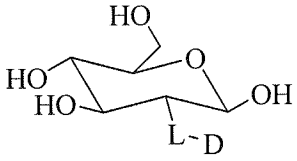
*International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007). Under *Graham*, the following factors should be considered: "(A) determine the scope and contents of the prior art; (B) ascertain the differences between the prior art and the claims in issue; (C) determine the level of ordinary skill in the pertinent art; and (D) evaluate any evidence of secondary considerations." *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Applicants have the burden to submit evidence of non-obviousness *only* if the Office has established a *prima facie* case of obviousness. *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984).

It is improper to use the specification as a blueprint in establishing a *prima facie* case of obviousness. *See In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) (holding that "[t]here must be a reason or suggestion in the art for selecting the procedure used, *other than the knowledge learned from the applicant's disclosure.*") (emphasis added).

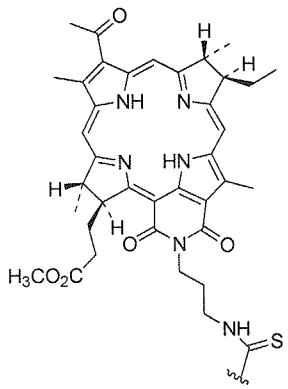
The Office has the burden of establishing a *prima facie* case of obviousness. It is respectfully asserted that the Office has not established a *prima facie* case of obviousness for at least the following reasons. In particular, the Office has not established that the claimed invention would have been a predictable variation of the cited references. The Office opines that, "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Pandey's porphyrin-carbohydrate conjugates to include 2-deoxyglucose as the carbohydrate and to include an isothiocyanate linker group, as taught by Tidmarsh." (Office Action, page 7.) The cited references, singly or combined, do not teach the invention of claim 1. Furthermore, the cited references,

singly or combined, do not provide a rationale to combine the disclosures of Pandey, Tidmarsh and Fukuzumi to arrive at the claimed invention.

The Office points specifically to compound 2b of Pandey as being structurally close to the compounds of claim 1. (Office Action, page 4.) Applicants respectfully disagree. The claimed invention encompasses a 2-deoxyglucose conjugate, which is represented by the formula:




wherein L is a linker group; and D is a photosensitive group such as BChlPP, illustrated below:



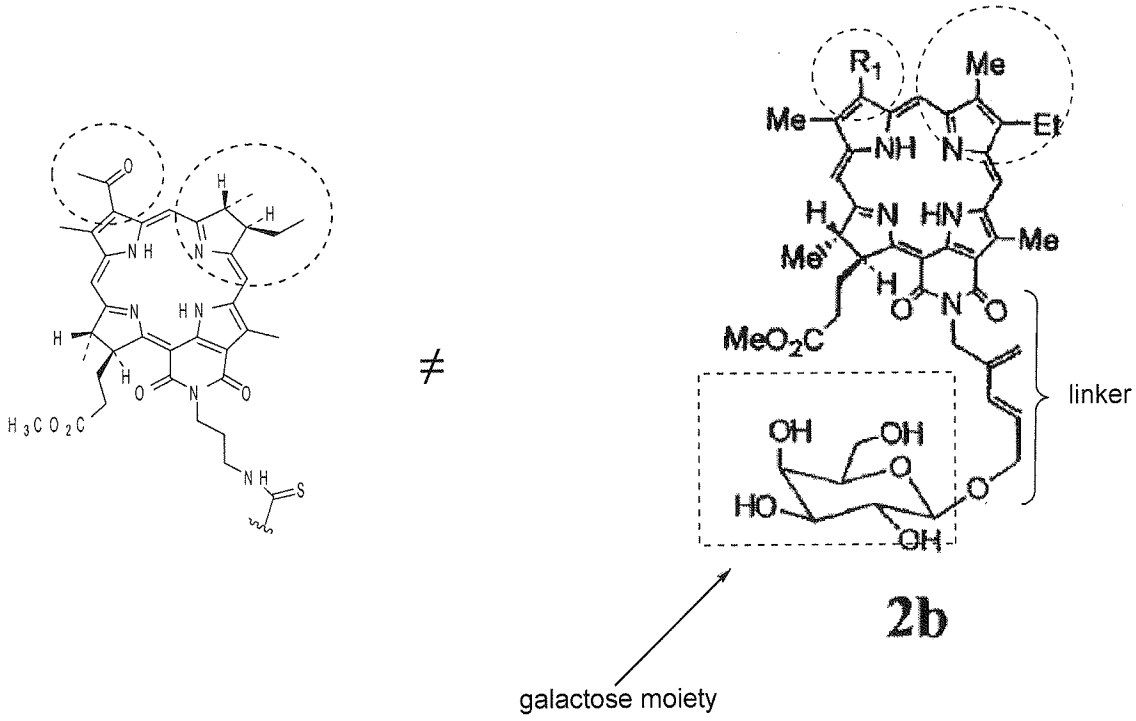

**BChlPP**

The propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) group bonded to the imido nitrogen is considered part of the BChlPP moiety.

Compound 2b of Fig. 17 markedly differs from the claimed compound in several important ways. First, the porphyrin moiety is not the same as, or structurally similar to, the porphyrin moiety of the BChlPP of claim 1 because, *inter alia*:

(i) the "$R_1$" moiety on the upper-left hand ring of the porphyrin moiety in Pandey can be a large number of moieties, ***none of which is the carbonyl moiety of the BChlPP of claim 1.*** (*See* Pandey, page 2, ¶ [0015]; and

(ii) the upper-right hand ring of the porphyrin moiety of compound 2b contains an additional double bond.




**BChlPP Conjugate** **Pandey's Compound 2b**

Second, the substituent at the imido nitrogen of compound 2b is also not the same as the propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) moiety at the imido-nitrogen of the

claimed compound. In addition, Pandey does not contain any reason or rationale to modify the group at the imido nitrogen to obtain the claimed group. Indeed, it is known from Fukuzumi that modifying specific substituents on the porphyrin moiety may alter the photophysical and electrochemical properties of the chlorin or bacteriochlorin moiety. (Fukuzumi, page 5106, left column, second full paragraph.)

Third, not only does Pandey not teach the photosensitive moiety ("D group") of the claimed invention, Pandey also does not teach the linker or the 2-deoxyglucose moieties. Pandey states that compounds containing a galactose or lactose saccharide are preferred. (Pandey, page 2, ¶ [0016].) In fact, a galactose moiety is used in compound 2b. In addition, the placement of the linkage on the carbohydrate moiety is not the same as the claimed invention. Notably, the linker is not directly bonded to the 3-position of the pyranose (six-membered) ring, as claimed. Instead, the linker is bonded to the 2-position of the pyranose (six-membered) ring. Pandey does not provide a reason or rationale to modify its compounds to arrive at the claimed compounds. Therefore, the Office has not established a sufficient rationale for combining the disclosures of Pandey, Tidmarsh and Fukuzumi to arrive at the claimed conjugates.

Tidmarsh does not cure the deficiencies of Pandey. It is respectfully asserted that the Office has clearly used hindsight to advance the obviousness arguments made in the present Office Action. Specifically, the Office has taken Applicants' disclosure as a blueprint to reconstruct the presently claimed invention from isolated pieces of cited art in contravention of the requirement that obviousness be judged from the perspective of a person having ordinary skill in the art *at the time the invention was made. See* 35 U.S.C. § 103. As noted, Pandey does not disclose the photosensitive moieties in the claims, the

linker group or the 2-deoxyglucose moiety. Tidmarsh does not disclose or even suggest use of bacteriochlorin compounds (such as BChlPP) in the conjugates described therein.

Further, Tidmarsh does not disclose modifying the compounds of Pandey, e.g., compound 2b, to arrive at the claimed compound. The Office, on page 8 of the Office Action, points to the following quotation of Tidmarsh as providing a rationale for arriving at a propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) group, as encompassed by the claimed invention:

> In one group of embodiments, L is a bond such that the fluorophore Fl is directly attached to Glc. Typically, this attachment is accomplished via coupling of a functional group on Fl with a compatible (e.g., linkage-forming) functional group on Glc. In certain preferred embodiments, Fl has an ***isocyanate, isothiocyanate [-N=C=S] or carboxylic acid functional group that is used to attach Fl to a hydroxy or amino group present on Glc to form a carbamate, thiocarbamate, urea or thiourea linkage between the components.***

Tidmarsh at col. 20, lines 47-56. (emphasis added)

Contrary to the Office's assertions, the preceding paragraph does not describe or suggest the propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) moiety of the claimed compound. Instead, Tidmarsh describes a large genus of possible linking groups with no specific description or suggestion that would lead a person having ordinary skill in the art to the claimed invention. (*See* Tidmarsh, col. 9, line 58 to col. 11, line 26). Furthermore, the Office on page 8 of the Office Action, points to the section of Tidmarsh, which states: "The length of the linker arm can be varied", as providing a rationale for arriving at a propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) group, as encompassed by the claimed invention. However, that statement without more would not lead a person of ordinary skill with propyl-thioamide (–$CH_2CH_2$-$CH_2$–NH-(C=S)-)

group much less to the claimed invention. For instance, the statement does not provide guidance as to what atoms/groups should be used to lengthen the linker, or even in what order they should be placed.

Regarding the placement of the linking group, Tidmarsh teaches placement of the linking group both the 2- and 3-positions of the 2-deoxyglucose moiety (cpd. Ia vs. Ic) as well as to a 2-deoxyglucose derivative. (*See* Tidmarsh, cols. 15-16). Therefore, Tidmarsh does not describe or suggest that the preferred bonding site for the linker is at the 2-position of the pyranose (six-membered) ring. As such, Tidmarsh does not provide rationale to combine the disclosures of Pandey, Tidmarsh and Fukuzumi to arrive at the claimed conjugates.

Fukuzumi does not cure the deficiencies of Pandey and Tidmarsh. As noted above, neither Pandey nor Tidmarsh teach the diagnostic moieties of the present invention. Fukuzumi also does not teach BChlPP or any other D-groups recited in claim 1. Fukuzumi's compound 3 at page 5108 differs from BChlPP of claim 1 in at least two ways: (1) stereochemistry of the chiral carbons of the upper-right-hand ring of the porphyrin moiety is different; (2) the "linker" substituent at the imido nitrogen is different (hexyl in compound 3 vs. (–$CH_2CH_2$-$CH_2$–NH-(C=S)-) in BChlPP). Nothing in Fukuzumi suggests changing the stereochemistry of these chiral carbons the upper-right-hand ring of the porphyrin moiety, or replacing the hexyl group of compound 3 with a propyl-thioamide group (–$CH_2CH_2$-$CH_2$–NH-(C=S)-), bonding that porphyrin-propylthioamide group to a nitrogen atom to form a thiourea linker, and bonding this linking group to a 2-deoxyglucose molecule to arrive at the claimed invention. Instead, Fukuzumi highlights the unpredictability insofar as modifying bacteriochlorin

compounds. (Fukuzumi, page 5106, left column, 2nd paragraph.) Specifically, Fukuzumi indicates that modifying specific substituents on the porphyrin moiety may alter the photophysical and electrochemical properties of the chlorin or bacteriochlorin moiety. (*Id.*)

Excluding replacement of the hexyl group on the imide-nitrogen, there are at least 20 different sites (see Figure 1 below) to which the 2-deoxy glucose molecule could be bonded, via a linking group, to compound 3 of Fukuzumi:

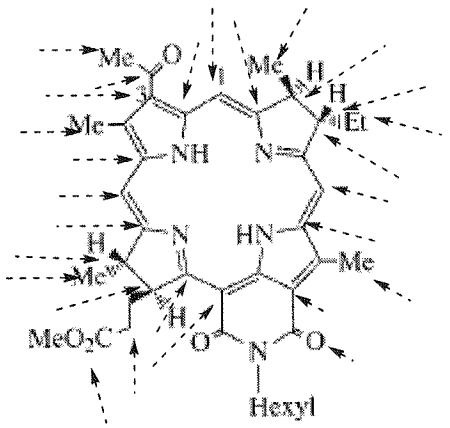



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***Figure 1***

Fukuzumi does not describe or suggest that the preferred bonding site is the nitrogen atom of the imide moiety. Furthermore, Fukuzumi does not disclose the use of bacteriochlorin compounds with 2-deoxy glucose. Therefore, the Office has not provided an adequate rationale to combine the disclosures of Pandey, Tidmarsh and Fukuzumi to arrive at the claimed conjugates. Absent this use of improper hindsight to pick and choose sections of the cited art to compare against the presently claimed

invention, the cited references cannot be properly combined in an attempt to make out a *prima facie* case of obviousness.

Based on the foregoing remarks, Applicants respectfully assert that the Office has not established a *prima facie* case of obviousness of the presently claimed invention. Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

## *Conclusion*

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: 9/20/2010

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